WHAT IS CLAIMED IS:

1. A method of screening for drug candidates useful in treating depression comprising:

(a) combining an assay solution with APAF1, or homolog, derivative, or fragment thereof, in the presence of a drug and the absence of said drug; and

(b) measuring the level of the biological activity of APAF1, or homolog, derivative, or fragment thereof, wherein if the level of the biological activity is less in the presence of said drug than in the absence of said drug then said drug is a drug candidate for treating depression.

2. The method of claim 1 wherein said biological activity is the ability to form a protein:protein interaction.

3. The method of claim 1 wherein said APAF1, or homolog, derivative, or fragment thereof, is a mutant APAF1.

4. The method of claim 3 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, is selected from the group consisting of: (a) a substitution at amino acid position 450; (b) a substitution at amino acid position 465; (c) a substitution at amino acid position 777; (d) a substitution at amino acid position 782 substituted; (e) a substitution at amino acid position 953; (f) a substitution at amino acid position 415; (g) a substitution at amino acid position 357; (h) a substitution at amino acid position 479; and (f) a substitution at amino acid position 625, all of which are in reference to SEQ ID NO:2.

5. The method of claim 3 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, is selected from the group consisting of: (a) Cys at position 450 substituted with Trp; (b) Gln at position 465 substituted with Arg; (c) Glu at position 777 substituted with Lys; (d) Asn at position 782 substituted with Thr; (e) Thr at position 953 substituted with Ala; (f) Leu at position 415 substituted with Pro; (g) Ser at position 357 substituted with Leu; (h) Asp at position 479 substituted with Glu; and (f) Glu at position 625 substituted with Ala, all of which are in reference to SEQ ID NO:2.

6. The method of claim 3 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, comprises the amino acid sequence as set forth in SEQ ID NO:3.

7. The method of claim 2, wherein said protein:protein is selected from the group consisting of APAF1:APAF1, APAF1:Cytochrome C, APAF1:procaspase-9, APAF1:caspase-9, APAF1:AT1.

8. The method of claim 1 wherein said biological activity is the ability of APAF1 to bind and/or hydrolyze ATP or dATP, or analogs thereof.

9. The method of claim 1, wherein said drug candidate is further tested in a cellular apoptosis model.

10. The method of claim 1, wherein said drug candidate is further tested in an animal depression model.

11. The method of claim 1, wherein said animal depression model is selected from the group consisting of: (a) the forced swim test, (b) the tail suspension test, (c) learned helplessness test, (d) chronic mild test stress, (e) social stress test, (f) early life stress test, (g) olfactory bulbectomy test, (h) fear conditioning test, (i) anxiety based tests, (j) reward based-tests, and (k) cognition tests.

12. The method of claim 2 wherein said protein:protein interaction is measured by a yeast two-hybrid assay.

13. A method of screening for drug candidates useful in treating depression resulting from an alteration in *APAF1*, said method comprising measuring the level of the biological activity of a mutant APAF1, or homolog, derivative, or fragment thereof, in both the presence of a drug and the absence of said drug, wherein if the level of the biological activity is less in the presence of said drug than in the absence of said drug then said drug is a drug candidate for treating depression.

14. The method of claim 13 wherein said biological activity is the ability to form a protein:protein interaction.

15. The method of claim 13 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, is selected from the group consisting of: (a) a substitution at amino acid position 450; (b) a substitution at amino acid position 465; (c) a substitution at amino acid position 777; (d) a substitution at amino acid position 782 substituted; (e) a substitution at amino acid position 953; (f) a substitution at amino acid position 415; (g) a substitution at amino acid position 357; (h) a substitution at amino acid position 479; and (f) a substitution at amino acid position 625, all of which are in reference to SEQ ID NO:2.

16. The method of claim 13 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, is selected from the group consisting of: (a) Cys at position 450 substituted with Trp; (b) Gln at position 465 substituted with Arg; (c) Glu at position 777 substituted with Lys; (d) Asn at position 782 substituted with Thr; (e) Thr at position 953 substituted with Ala; (f) Leu at position 415 substituted with Pro; (g) Ser at position 357 substituted with Leu; (h) Asp at position 479 substituted with Glu; and (f) Glu at position 625 substituted with Ala, all of which are in reference to SEQ ID NO:2.

17. The method of claim 13 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, comprises the amino acid sequence as set forth in SEQ ID NO:3

18. A method of screening for drug candidates useful in treating depression resulting from an alteration in *APAF1*, wherein said method comprises treating an transgenic animal which is heterozygous or homozygous for *APAF1* containing an alteration with a drug wherein if said animal does not develop depression then said drug is a drug candidate for treating depression.

19. The method of claim 18 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, is selected from the group consisting of: (a) a substitution at amino acid position 450; (b) a substitution at amino acid position 465; (c) a substitution at amino acid position 777; (d) a substitution at amino acid position 782 substituted; (e) a substitution at amino acid position 953; (f) a substitution at amino acid position 415; (g) a substitution at amino acid

position 357; (h) a substitution at amino acid position 479; and (f) a substitution at amino acid position 625, all of which are in reference to SEQ ID NO:2.

20. The method of claim 18 wherein said mutant APAF1, or homolog, derivative, or fragment thereof, is selected from the group consisting of: (a) Cys at position 450 substituted with Trp; (b) Gln at position 465 substituted with Arg; (c) Glu at position 777 substituted with Lys; (d) Asn at position 782 substituted with Thr; (e) Thr at position 953 substituted with Ala; (f) Leu at position 415 substituted with Pro; (g) Ser at position 357 substituted with Leu; (h) Asp at position 479 substituted with Glu; and (f) Glu at position 625 substituted with Ala, all of which are in reference to SEQ ID NO:2.